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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/722,205	11/25/2003	Stephen Alistair Smith	P31831C2	6787

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EXAMINER	
WILLIAMS, LEONARD M	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 05/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/722,205	SMITH, STEPHEN ALISTAIR	
	Examiner	Art Unit	
	Leonard M. Williams	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Examiner notes that claims 1-15 have been cancelled and new claims 16-35 added as per the preliminary amendment received 11/25/2003. Claims 16-35 will be evaluated based on their merits.

This application is a continuation of 09/928326 now abandoned, which is a continuation of 09/445858 now abandoned, which is the national stage entry of PCT/EP98/03692.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 16-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hofman et al. (New Oral Thiazolidinedione Antidiabetic Agents act as Insulin Sensitizers, Diabetes Care, volume 15, number 8, August 1992) in view of Fukuda et al. (A Clinical Study of a New Hypoglycemic Agent, Troglitazone, in Type 2 Diabetes Patients who are Unsatisfactorily-Controlled with Insulin, J. Clin.Ther. Med., Volume 11, number 10, October 1995) and further in view of Pool et al. (US Patent No. 5741803).

Hofman et al. teaches, on page 1075 column 2-3, that thiazolidinediones represent a new class of antidiabetic compounds (including troglitazone, rosiglitazone, etc.) that act as insulin sensitizers overcoming insulin-resistance. Hofman et al. teach, on page 1077 column 2, that in patients with concomitant impairment of both insulin secretion and insulin action, it may be possible to treat with two or more agents exerting complementary corrective actions. Patients with severely impaired pancreatic functions may benefit from a combined insulin sensitizer (such as a thiazolidinedione compound) and insulin dual therapy.

Hofman et al. does not teach the specific thiazolidinedione compound rosiglitazone in conjunction with insulin for the treatment of diabetes mellitus and conditions associated with diabetes mellitus, any particular dosage or dosage forms of the thiazolidinedione compounds, that the thiazolidinedione compounds can be administered as salts or hydrates, or that the thiazolidinedione compounds can be administered concomitantly with insulin or sequentially.

Fukuda et al. teach, on page 1, that 17 patients with insulin treated non-insulin dependent diabetes that were suffering from unsatisfactory glycemic control were

successfully treated with a combination therapy of insulin and an oral thiazolidinedione compound (troglitazone, 400mg per day for 12 weeks). Fukuda et al teach on page 4 that the dosage of insulin was not increased in any patient during the study but that two patients had to have their insulin dosages lowered due to mild hypoglycemia associated with the thiazolidinedione/insulin combination therapy. Fukuda et al., on page 12, state "...from the results obtained...an extensive application of the drug in insulin therapy, i.e., the use in uncontrollable cases by single agent of insulin and possible reduction of the dosage of insulin, was suggested."

Pool et al. teach, in the abstract, a compound of formula I or a tautomeric form thereof and/or a pharmaceutically acceptable solvate thereof for use in treating hyperglycemia. Pool et al. teach, in column 2 lines 5-55, that a preferred compound of formula I is 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]thiazolidine-2,4-dione maleic acid salt (rosiglitazone, a thiazolidinedione compound and the compound presented in the current application). Pool et al. teach in column 5 lines 1-43, that the compounds are particularly suitable for oral administration via unit dosage forms such as tablets and capsules and that the compounds can be administered 1-6 times a day such that the daily dose for a 70kg human will be in a range from 0.1-6000mg and more preferably 1-1500mg.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a thiazolidinedione compound concurrently with insulin as both the thiazolidinedione class of antidiabetic compounds were known and insulin was known and both have been used to treat diabetes.

The examiner respectfully points out the following from MPEP 2144.06: "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re* Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

One of ordinary skill in the art would have been motivated to do so in order to lower the amount of insulin needed for treatment of the diabetes patient as indicated and suggested by the results of Fukuda et al. The use of the Pool et al. compounds is obvious as it is from the same class of compounds as troglitazone (used by Fukuda et al., a thiazolidinedione compound), acts through the same mechanism, and achieves similar results. It would be obvious to use the Pool et al. compounds in a manner similar to the other thiazolidinedione compounds, i.e., in a combination therapy with insulin as suggested and exemplified by Hofman et al. and Fukuda et al. and one of ordinary skill in the art at the time the invention was made (without evidence to the contrary) would be expected to be able to formulate a dosing regimen of 1-2 times a day with a unit dosage of 1-12mg per unit dose and delivered either concurrently or sequentially with insulin to a patient in need thereof.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leonard M Williams whose telephone number is 571-272-0685. The examiner can normally be reached on MF 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

LMW

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER